REMARKS

The Invention is Enabled

Claims 1, 6-7, 9 and 15 have been rejected under 35 U.S.C. § 112, first paragraph. The Examiner has asserted the instant Specification as originally filed fails to disclose or describe step (d) of Claim 1, measuring the phosphorylation activity of the Src protein following contacting a cell with a candidate agent in the presence of APP. The Examiner has admitted the instant Specification as filed does provide support for an assay comprising the steps of (a) providing a Src protein and (b) determining if a compound inhibits the activity of the Src protein. The Examiner has also admitted the instant Specification discloses the results of an experiment wherein APP was added, via transfection of App-encoding vectors, to cells expressing Src and wherein the amount of APP_{sec} (the α-secretase product of APP) was measured in the presence and absence of Src; see Example 2 spanning pp. 9-10 of the instant Specification. However, the Examiner believes the instant Specification as originally filed does not provide support for screening methods comprising measuring the degree of Src phosphorylation activity in an assay where both APP and a candidate compound are present.

This rejection is respectfully traversed. On page 7, lines 19-29 of the instant Specification, it is clearly stated:

> The ***new*** results demonstrate that APP is phosphorylated not only by Abl. In fact Src kinase is also responsible for APP tyrosine phosphorylation. It is expected that tyrosine phosphorylation of APP alters the binding properties of its cytodomain, and then the processing of APP could be consequently modified. If so, this will prove useful the use of currently available tyrosine kinase inhibitors, and to design new ones for pharmacological modulation of the release of APP processing products in cellular and animal models of Alzheimer's disease.

> Taken together, the results from the following examples suggest that exogenous Src activity is responsible for activation of a pathway resulting in increased Aβ secretion.

This passage of the instant Specification clearly makes clear that a tyrosine kinase inhibitor, i.e. a candidate compound, and APP are both present, and further that the processing of APP is clearly a barometer regarding the activity of the candidate compound's ability to modulate the activity of Src kinase. Thus, contrary to the Examiner's assertions, the instant Specification readily enables Claims 1, 6-7, 9 and 15, and this rejection should be withdrawn.

In addition, the Examiner has asserted original Claim 8, in particular Step (c), is drawn to measurement of the activity of the Src in response to a candidate compound. In the Examiner's opinion though, neither original Claim 8 nor original Claim 1, upon which Claim 8 depends, allowed for inclusion of APP in the assay as well. Moreover, the Examiner contends the instant Specification as originally filed indicates that measuring the degree of tyrosine phosphorylation of APP, the specific form of Src phosphorylation activity recited in Claim 15, should not be performed as "[t]he mechanism by which active Src elicits such a dramatic increase in Aβ secretion is not clear." The Examiner contends the mechanism might depend on phosphorylation of some other proteins, different from APP, since, in the Examiner's opinion, tyrosine phosphorylation of APP by Abl-PP does not result in increased Aβ levels. It is also the Examiner's position the instant Specification as originally filed fails to disclose screening assays wherein the degree of Src-dependent phosphorylation is measured. In the Examiner's opinion, the instant Specification as originally filed points the public away from such a step. Yet, the Examiner admits the instant Specification as originally filed mentions that APP can be tyrosine-phosphorylated as recited in Claim 15.

In a previous response, it was argued to the Examiner the instant Specification provides support for the specific step of measuring tyrosine phosphorylation of APP by Src at page 7, lines 19-20 of the instant Specification as originally filed. The Examiner though believes this is a conclusory statement as to a possible activity of Src and not an indication of a step to be performed in a screening assay. It is the position of the Examiner that screening assays are discussed generally on page 5 of the instant Specification, but not at page 7, lines 19-20. Also, the Examiner contends the instant Specification fails to disclose assays conducted in the presence of both Src and App wherein Src phosphorylation in general as recited in Claim 1, or tyrosine phosphorylation of APP as recited in Claim 15, are measured in the presence of a candidate compound.

This rejection is respectfully traversed. Contrary to the Examiner's belief, screening assays are not "discussed generally" only on page 5 of the instant Specification. Rather, assays of the instant Invention are discussed on pages 5-8. Indeed, on page 7, lines 27-31 and on page 8, lines 1-5 of the instant Specification, it is clearly stated that:

> Taken together, the results from the following examples suggest that exogenous Src activity is responsible for activation of a pathway resulting in increased Aβ secretion. This also suggests that PP2 could be used as a pharmacological agent able to reduce Aβ secretion in cellular and animal systems resembling AD status.
>
> Therefore, a line of CHO cells stably overexpressing APP751 form was used, which secretes discrete levels of Aβ. If secretion involves endogenous Src activity, PP2 should be able to inhibit production of Aβ also in this cellular system.

This passage makes clear that APP and a candidate compound, e.g. PP2 are clearly present together in an assay of the instant Invention. Moreover, Examples 2 and 3 on pages 9 and 10 of the instant Specification also make clear that an inhibitor compound and APP are present together in an assay of the instant Invention. In Example 2 on page 9, HEK293 cells

were genetically modified to express APP. In Example 3, those genetically modified cells were exposed to PP2. It is clearly explained that:

> ...the rise in Aβ levels does depend on the tyrosine kinase activity of Src, since the accumulation of Aβ is sensitive to treatment by the Src-family specific inhibitor PP2. In fact, as shown in Figure 5, the exposure of transfected cells for 48 hours to increasing concentrations of PP2 results in dose-dependent decrease of secreted Aβ. Either PP3, an inactive analog of PP2, or vehicle alone, do not affect Aβ rise by SrcYF transfection.

(Page 10, lines 23-27 of the instant Specification).

Thus, contrary to the Examiner's assertion, page 5 is not only portion of the Specification that discusses assays of the instant Invention. As the passages of the Specification quoted above clearly demonstrate, enabling support can be found throughout the instant Specification. In *Callicrate v. Wadsworth Mfg., Inc.*, 427 F.3d 1361, 77 USPQ2d 1041 (Fed. Cir. 2005), the Federal Circuit made clear that any part of the specification can support an enabling disclosure, even a background section.

Furthermore, the Examiner is incorrect in asserting that the passage on page 7 of the instant Specification is merely a conclusory statement as to a possible activity of Src and not an indication of a step to be performed in a screening assay. The passages discussed above clearly demonstrate that the passage on page 7 is indeed not merely conclusory, but rather readily provides enabling support to Claims 1, 6-7, 9 and 15 of the instant Specification.

Thus, for all of the foregoing reasons, it is respectfully submitted these rejections have been obviated and they should be withdrawn.

Specification

The Examiner has objected to the amendment to the Specification filed June 12, 2008, asserting it introduces new matter into the instant Disclosure. The Examiner contends the added material which is not supported by the original disclosure is as follows:

Applicant changed the sentence beginning at page 6, line 11 from:

"b) determining if a compound inhibits the expression of Src protein."

to:

"b) determining if a compound inhibits the activity of Src by measuring the activity of said Src protein in response to said candidate compound."

In the Examiner's opinion, the Specification as originally filed only contemplated determining if expression of Src protein was changed in assays wherein step a) is "providing a sequence which regulates Src". The Examiner has asserted the proposed amendment changes the Disclosure from determining if expression is changed to determining if activity is changed.

The Examiner has required Applicant to cancel the alleged new matter in instant Amendment.

In the instant Amendment, the Specification has been amended to place it in the condition it was in prior to the Amendment filed June 12, 2008. Hence, this objection should be withdrawn.

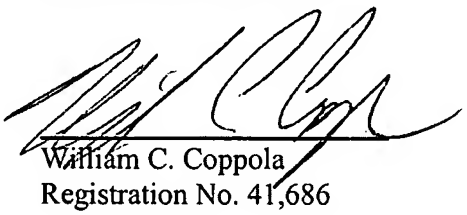
Fees

No fees are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 18-1982 for any underpayment, or to credit any overpayments.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,



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